IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:

Manne Satyanarayana REDDY et al.

Application No.: 10/716,200 Art Unit 1625

Filed: November 18, 2003 Examiner: Patricia L. Morris

For: CRYSTALLINE ESOMEPRAZOLE COMPOUNDS AND PROCESS FOR THE PREPARATION THEREOF

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

BRIEF ON APPEAL

Sir:

Further to the Notice of Appeal filed on August 9, 2007 for the subject application, a brief in support of the appeal is now submitted. Submission of a brief in support of the appeal in this case is due by October 9, 2007. Accordingly, this brief is being timely filed.

1. Real Party in Interest

The real parties in interest are Dr. Reddy's Laboratories Limited and Dr. Reddy's Laboratories, Inc., assignees of the application from the inventors/appellants.

2. Related Appeals and Interferences

There are no appeals or interferences that are related to this appeal, or which will affect or have a bearing on this appeal.

3. Status of the Claims

Claims 1, 3-9, 11-17, 33 and 34 were finally rejected in an Office Action mailed on May 10, 2007, and are the subject of this appeal. Claims 19-32 have been withdrawn from consideration following a restriction requirement, and can be considered as canceled without prejudice to presentation in a continuing application. Claims 2, 10 and 18 were previously canceled.

4. Status of Amendments

An Amendment After Final was filed on July 20, 2007, subsequent to final rejection. No claims were amended, canceled or added. The Examiner indicated in an Advisory Action mailed July 26, 2007, that the request for consideration was considered but did not place the application in condition for allowance for reasons clearly set forth in the record.

5. Summary of Claimed Subject Matter

The claimed subject matter encompasses crystalline form II of esomeprazole magnesium trihydrate.

Independent claim 1 is directed to a compound which is a crystalline form II of esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1. (Instant specification, page 6, lines 4-7.)

Independent claim 6 is directed to a composition comprising esomeprazole magnesium, wherein at least 75% of the esomeprazole magnesium is a crystalline form II of esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1. (Instant specification, page 2, lines 6-8.)

Independent claim 33 is directed to a solid pharmaceutical composition comprising a crystalline form II of esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1 and a pharmaceutically acceptable carrier. (Instant specification, page 11, lines 26-34.)

Independent claim 34 is directed to a method for reducing gastric acid secretion in a subject comprising administering to said subject a solid pharmaceutical composition comprising a therapeutically effective amount of a crystalline form II of esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1. (Instant specification, page 14, lines 1-15.)

The dependent claims are directed to various embodiments of the disclosed compound and compositions.

A copy of the appealed claims is appended hereto, beginning at page 18.

6. Grounds of Rejection to be Reviewed on Appeal

a. Whether claims 1, 3-9, 11-17, 33 and 34 are anticipated under 35 U.S.C. §§ 102(a) and/or (e) by Cotton et al (U.S. Pat. No. 6,369,085; "Cotton").

b. Whether claims 1, 3-9, 11-17, 33 and 34 are unpatentable under 35 U.S.C. § 103(a) over Cotton in view of Bohlin et al. (U.S. Pat. No. 6,162,816; "Bohlin"); Lindberg et al. (U.S. Pat. No. 6,875,872; "Lindberg"), Haleblian et al. (*J. Pharm. Sciences*, (1969), 58 pp. 911-929; "Haleblian"), Muzaffar et al. (*J. of Pharmacy* (Lahore) 1979, 1(1), 59-66; "Muzaffer"), Chemical & Engineering News, Feb. 2003 ("C&E News"), U.S. Pharmacopia, 1995, pp. 1843-1844 ("USP") and Concise Encyclopedia Chemistry, pages 872-873 (1993) ("CEC").

c. Whether claims 33 and 34 are invalid under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement.

7. Argument

a. Rejection Under 35 U.S.C. §§ 102(a) and/or (e)

Claims 1, 3-9, 11-17, 33 and 34 stand finally rejected under 35 U.S.C. §§ 102(a) and/or (e) as allegedly anticipated by Cotton. According to the Examiner, Cotton specifically discloses the instant compound. Particular attention is directed to Example 1 and column 2, lines 47-50, which states that "[t[he compound of the invention is characterized by being highly crystalline, i.e. having a higher crystallinity than any other form of magnesium salt of S-omeprazole disclosed in the prior art.

It has long been the law that anticipation can properly be held only where a prior art document teaches each and every limitation of the rejected claim. *See Verdegaal Bros. v. Union Oil Co. of Cal.*, 814 F.2d 628, 631 (Fed. Cir. 1987). Here, each of the rejected claims is directed to a crystalline form II of esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1 of the instant

specification. Applicants submit that under *Verdegaal*, it is error for the Examiner to ignore the X-ray diffraction limitation in attempting to make out a case of anticipation.

Cotton discloses esomeprazole magnesium trihydrate having an X-ray diffraction pattern distinctly different from that of the instantly claimed compound. For example, even a cursory inspection reveals that the X-ray diffraction pattern for crystalline form II of esomeprazole magnesium trihydrate of the instant claims shows, *inter alia*, very prominent peaks at about 4.8 and 18.5 angstroms that are completely absent from the pattern for the esomeprazole magnesium trihydrate disclosed in Cotton, while the X-ray diffraction pattern for the esomeprazole magnesium trihydrate of Cotton shows, *inter alia*, a very prominent peak at about 22.5 degrees two-theta that is completely absent from the pattern for the instant crystalline form II of esomeprazole magnesium trihydrate. *Compare* Fig. 1 and the table at page 6 of the instant specification with Fig. 1 of Cotton. Thus, there is no teaching, or even a suggestion, in Cotton of crystalline form II of esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1 of the instant specification. As such, Cotton cannot anticipate the claimed invention, and the rejection should not be sustained.

According to the Examiner, the differences in X-ray diffraction patterns are not persuasive because such patterns alone do not demarcate the identity of two products. The examiner cites to Davidovich et al., *Am. Phar. Rev.* 7:16 (2004) ("Davidovich") for the proposition that small changes in XRPD patterns can arise as experimental artifacts rather than polymorphism. As evidence of this phenomenon, the Examiner cites to Figures 4.21 and 8.5 of Bernstein, "Polymorphism in Molecular Crystals," pp. 118, 272 (2002) ("Bernstein") as showing that the same compound can have two different X-ray

diffraction patterns. However, rather than supporting the Examiner's position, Davidovich and Bernstein actually support the conclusion that the instant crystalline form II of esomeprazole magnesium trihydrate and the esomeprazole magnesium trihydrate disclosed in Cotton are distinct polymorphic forms.

First, although Davidovich does state that changes in X-ray diffraction patterns can arise from experimental artifacts, such changes are said to be "small." (Abstract, p. 10.) An examination of Figures 2, 3, 5, 6 and 8-10 demonstrates just how small these changes are. In contrast, a comparison of the X-ray diffraction data previously described regarding the instant crystalline form II of esomeprazole magnesium trihydrate and the esomeprazole magnesium trihydrate disclosed in Cotton demonstrates quite large changes in X-ray diffraction patterns, even allowing for standard error in measurement. Such large differences between the X-ray diffraction patterns for the esomeprazole magnesium trihydrate disclosed in Cotton and the instant crystalline form II of esomeprazole magnesium trihydrate are simply not the type of minor variation contemplated by Davidovich as being due to artifacts rather than true polymorphism. Indeed, Davidovich states that "Powder X-ray Diffraction (PXRD) is a powerful tool in identifying different crystalline phases by their unique diffraction patterns." (p. 10.)

Second, although Figure 4.21 of Bernstein does show different X-ray diffraction patterns for sulphathiazole, this example is admittedly "dramatic." (p. 117.) More importantly, Fig. 4.21 does not compare two different powder diffraction patterns, but rather a powder diffraction pattern with an expected pattern calculated from the crystal structure. This explains the conclusion of Bernstein that "almost all of the expected diffraction peaks have been severely suppressed." (*Id.*) The Examiner has provided no

evidence or reasoning why such peak suppression would be expected when comparing actual powder diffraction patterns between different esomeprazole magnesium trihydrate preparations.

Regarding Figure 8.5 of Bernstein, the Examiner describes the figure by saying that "[a]lthough there are new peaks, the authors concluded that "it may not be a pure modification", i.e., not a true polymorph." However, Figure 8.5 of Bernstein actually states that "[t]he lower pattern [for Pigment Yellow 17] shows evidence of virtually every peak that appears in the upper pattern [for Pigment Yellow 17], indicating that it may not be a pure modification. Nevertheless, there are diffraction maxima that do appear to be unique to a second form." (p. 273) (emphasis added.) Thus, the authors actually conclude that the Pigment Yellow 17 in Figure 8.5 existed as an unpure mixture of two different polymorphs, not, as the Examiner asserts, a single form having two different XRPD patterns. This is confirmed by the authors' statement on p. 273 that Pigment Yellow 17 is a "dimorphic system, for which both powder patterns are shown in Fig. 8.5."

Thus, contrary to the Examiner's position, both Davidovich and Bernstein support the use of X-ray diffraction analysis to establish polymorphic identity. As noted by Brittain, ed. (Polymorphism in Pharmaceutical Sciences, 1999, p. 235) (of record):

> [D]uring the most common evaluation of drug substances, it is usually sufficient to establish only the polymorphic identity of the solid and to verify that the isolated compound is indeed of the desired structure. For these reasons, the technique of X-ray powder diffraction (XRPD) is the predominant tool for the study of polycrystalline material and is eminently suited for the routine characterization of polymorphs and solvates.

Thus, consistent with the references of record, the major differences in X-ray diffraction patterns indicate that the instant crystalline form II of esomeprazole magnesium trihydrate and the esomeprazole magnesium trihydrate disclosed in Cotton are indeed distinct polymorphic forms. As such, the Examiner has failed to make out a *prima facie* case for anticipation of the claimed form. *See Ex parte Havens*, Appeal No. 2001-0091 for U.S. Pat. Appl. No. 08/732,254, now U.S. Pat. No. 6,452,007 (BPAI 2001) ("The examiner has provided no evidence or scientific reasoning to show that the delavirdine mesylate disclosed and claimed [in the prior art reference] is in the [claimed] crystal form. Therefore, the examiner has not made out a *prima facie* case of anticipation by inherency.").

Accordingly, Applicants submit claims 1, 3-9, 11-17, 33 and 34 are not anticipated by the cited art, and the rejection should not be sustained.

b. Rejection Under 35 U.S.C. § 103(a)

Claims 1, 3-9, 11-17, 33 and 34 stand finally rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Cotton in view of Bohlin, Lindberg, Haleblian, Muzaffar, C&E News, USP and CEC. According to the Examiner, Cotton teaches the crystalline form of the magnesium salt of esomperazole. Bohlin and Lindberg are said to teach that esomeprazole and its salts can exist in different crystalline states. Muzaffar and Haleblian are said to teach that compounds can exist in amorphous forms as well as crystalline states. C&E News, USP and CEC are said to teach that at any particular temperature and pressure, only one crystalline form is thermodynamically stable. Thus, according to the Examiner, it would appear to one skilled in the art in view of the

references that the instant compound would exist in different crystalline forms. No unexpected or unobvious properties were noted by the Examiner.

The standards for making an obviousness rejection per § 103(a) are summarized in MPEP § 706.02(j) as follows:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck,* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

As discussed above, Cotton discloses a crystalline form of esomeprazole magnesium trihydrate, but does not teach or suggest crystalline form II of esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1 of the instant specification. Similarly, Bohlin discloses that esomeprazole base can exist in amorphous, partly crystalline or substantially crystalline solid states, while Lindberg discloses crystalline esomeprazole magnesium, but neither teachs or suggests crystalline form II of esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1 of the instant specification. The ancillary references cited by the Examiner merely provide general background information relating to the study and preparation of polymorphs or case histories of specific polymorphic compounds (none of which is esomeprazole magnesium trihydrate), and thus add nothing over the primary references. As such, none of the cited references, alone or in

combination teach or suggest the instantly claimed compound with all its limitations. This alone is enough to overcome the Examiner's obviousness rejection. *See Ex parte Havens, supra* ("The examiner's obviousness rejection seems to suffer the same infirmity as her anticipation rejection . . . . The examiner has provided no evidence or convincing reason why the prior art disclosure of delavirdine mesylate in an undefined state would have suggested the specific S and T crystal forms that are the subject of the instant claims.") (emphasis added).

Contrary to the Examiner's position, the proper test for obviousness in this case is not whether the existence of esomeprazole magnesium trihydrate polymorphs is suggested by the prior art, but whether it would have been obvious to make the particular esomeprazole magnesium trihydrate claimed in the instant application based on the prior art:

> The law of § 103 requires quite a different inquiry from that conducted by the ALJ. Thee correct inquiry is not whether the Bouzard monohydrate [polymorph] could have been produced by manipulation of other cefadroxil processes, once the existence of the Bouzard monohydrate was known. The question is whether it would have been obvious to make the Bouzard monohydrate, based on the prior art.

Bristol-Myers Co. v. U.S. Int'l Trade Comm'n, 892 F.2d 1050, 1989 WL 147230 (Fed. Cir. Dec. 8, 1989) (unpublished decision) (emphasis added).

Here, the references cited by the Examiner suggest at most the possibility of other esomeprazole magnesium trihydrate polymorphs. The Examiner has pointed to nothing in the cited references, however, that would suggest to one skilled in the art the particular form claimed in the instant application. *See Ex parte Andrews*, Appeal No. 2002-0941 for U.S. Pat. Appl. No. 09/166,445, now U.S. Pat. No. 6,713,481 (BPAI 2003) ("[T]he

examiner has not adequately explained how a person having ordinary skill would have been led from 'here to there,' i.e., from the [prior art] compound having formula I to the crystalline polymorph form I recited in claims 1 through 5."); *Ex parte Portmann*, Appeal No. 2003-1199 for U.S. Pat. Appl. No. 09/125,329, now U.S. Pat. No. 6,740,669 (BPAI 2004) (same). Indeed, CEC, p. 32, cited by the Examiner, states that "no method yet exists to predict the polymorphs of a solid compound with significant certainty."

Similarly, the Examiner has pointed to nothing in the cited references that would suggest to one skilled in the art a process for preparing the particular esomeprazole magnesium trihydrate claimed in the instant application, or a reasonable likelihood of success. *See Ex parte Gala*, Appeal No. 2001-0987, U.S. Pat. Appl. No. 09/169,109, now U.S. Pat. No. 6,335,347 (BPAI 2002) ("Applicants have discovered specific solvents and experimental conditions, producing a distinctly different polymorph form 2 loratidine . . . . This information stems from applicants' specification, but not from the cited prior art".); *Ex parte Polniaszek*, Appeal No. 2001-1805, U.S. Pat. Appl. No. 08/732,254, now U.S. Pat. No. 6,452,007 (BPAI 2003) ("The prior art relied upon by the examiner does not teach this specific polymorph as claimed by the appellants. The Examiner failed to demonstrate that the prior art even recognized that the claimed compound exists in different polymorphic forms, or that there is a known or obvious way to manufacture the specific polymorphic form claimed.").

In an effort to circumvent the deficiencies of the cited art, the Examiner relies on *In re Cofer* and *Ex parte Hartop*:

> [A]s set forth by the court in In re Cofer 148 USPQ 268, Ex parte Hartop 139 USPQ 5252, that a product which are merely different forms of known compounds, notwithstanding that some desirable results are obtained

> thereform, are unpatentable. The instant claims are drawn to the ***same pure substance*** as the prior art that only having *different arrangements and or different conformations of the molecule*. A mere difference in physical property is a well known conventional variation for the same pure substance is prima facie obvious. (Emphasis in original.)

Thus, the Examiner appears to be taking the position that new polymorphs are *per se* unpatentable over the originally identified compound or previously identified polymorphs of the same compound. Such a rule, however, is inconsistent with the law on obviousness. *See Ex parte Andrews*, *supra* (quoting *In re Ochiai*, 71 F.3d 1565 (Fed. Cir. 1995) ("The use of *per se* rules flouts § 103 and the fundamental case law applying it. . . . [R]eliance on *per se* rules of obviousness is legally incorrect and must cease.").

The Examiner's reliance on *Cofer* and *Hartop* are misplaced in this case. *Cofer* actually held the claimed crystalline 2,2-bis patentable because

> [T]he board failed to address . . . whether the prior art suggests the particular structure or form of the compound or composition as well as suitable methods of obtaining the structure or form. (Emphasis added.)

354 F.2d 664, 668 (CCPA 1966). The *Cofer* court addressed the *Hartop* decision, which had been relied upon by the board in finding the claimed crystalline 2,2-bis unpatentable:

> We think examination of the decisions relied on . . . in *Hartop* will demonstrate that the materials involved therein were found unpatentable where the alleged difference in form or purity of those substances was either disclosed or inherent therein. (Emphasis added.)

Id. at 667. Here, as discussed above, the references cited by the Examiner neither disclose or suggest the particular esopmeprazole magnesium trihydrate disclosed and claimed in the instant application.

The Board of Patent Appeals & Interferences has recently cautioned against the reliance on *Hartop* in polymorph cases. As stated in *Ex parte Gala*, *supra*:

> The examiner relies heavily on this proposition of law set forth in *Ex parte Hartop* . . . : "[m]erely changing the form, purity or another characteristic of an old product, the utility remaining the same as that for the old product, does not render the claimed product patentable." According to the examiner, polymorph form 2 loratadine is merely another form of an old product (polymorph form 1 loratadine) and both forms possess the same utility. Accordingly, the examiner concludes that applicants' claims, reciting polymorph form 2 loratadine, are unpatentable. We disagree. Here, we invite attention to *In re Cofer* . . . , where the court substantially discredited PTO reliance on the above-quoted proposition of law in *Hartop*. Like the situation presented in *Cofer*, the examiner in this case has not adequately established that the prior art (1) suggests the polymorph form 2 of loratadine; or (2) discloses or renders obvious a method for making the polymorph form 2 of loratadine. (Emphasis added.)

See also Ex parte Andrews, *supra* ("[T]he principal of law enunciated in *Ex parte Hartop* . . . has been substantially discredited in *In re Cofer* . . . ."); *Ex parte Portmann*, *supra* (same).

According to the Examiner, Applicants do not point to any objective evidence which demonstrates that the claimed compound exhibits any properties which are actually different from the closest prior compounds. Applicants respectfully submit that such differences need not be demonstrated because a *prima facie* case of obviousness has not been made under the proper test described above. The CCPA in *In re Grose* specifically rejected the application of the law of structural obviousness, and hence a requirement for a showing of unexpected properties, when analyzing the patentability of new solid state forms:

> No reason exists for applying the law relating to structural obviousness of those compounds which are homologs or isomers of each other to this case. . . . A zeolite, like those of the instant case, is not a compound which is a homolog or isomer of another, but is a mixture of various compounds related to each other by a particular crystal structure. Moreover, no other chemical theory has been cited as a basis for considering appellants' zeolite as prima facie obvious in view of [the prior art] zeolite R.

592 F.2d 1161, 1167-68 (CCPA 1979).

Accordingly, Applicants submit that claims 1, 3-9, 11-17, 33 and 34 are not obvious over the cited art, and the rejection should not be sustained.

c. Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 33 and 34 stand finally rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. According to the Examiner, there is a lack of description as to whether the compositions are able to maintain the compound in the amorphous form. In particular, the Examiner states that processing a compound into a pharmaceutical composition could create a different form. Furthermore, the Examiner states that administering a compound to a subject results in the loss of crystalline structure.

Claims 33 and 34 are directed to a solid pharmaceutical composition comprising crystalline form II of esomeprazole magnesium trihydrate having substantially the same XRPD pattern as shown in Fig. 1 of the instant specification, and a method for reducing gastric acid secretion in a subject comprising administration of such a solid pharmaceutical composition. The claims contain no limitation requiring that the crystalline form be maintained indefinitely, or that it be the only form present, and Applicants submit that it is error to read the claims as such. Any esomeprazole

magnesium trihydrate not having substantially the same X-ray diffraction pattern as shown in Figure 1 is simply outside the scope of the claims.

The instant specification clearly describes and enables the preparation of compositions comprising crystalline form II esomeprazole magnesium trihydrate having substantially the same X-ray diffraction pattern as shown in Fig. 1 of the instant specification, and methods of treatment comprising the same. *See, e.g.*, page 11, line 26 to page 15, line 12. In addition, the specification clearly describes and enables methods for identifying and monitoring the presence of crystalline form II esomeprazole magnesium trihydrate in the claimed composition before, during and after its preparation. *See, e.g.*, page 5, line 32 to page 9, line 22.

Furthermore, Applicants note that several of the references of record cited by the Examiner explain that polymorphic transformation can be very slow (on the order of years) owing to the relative stability of the metastable form. For example, Muzaffar notes at page 60:

> When the rate of conversion of a metastable form is so slow as to be negligible, the solubility of the compound will be maximal and will have a faster rate of dissolution and hence absorption. This biopharmaceutical property of the polymorphs could be explained for achieving better results in the formulation of drugs, especially in the unit disage forms of the drugs.

Thus, even assuming that crystalline form II esomeprazole magnesium trihydrate is a metastable form (mere conjecture at this point), its possible transformation at some point in the future does not detract from its utility while in the claimed form. Again, any esomeprazole magnesium trihydrate not having substantially the same X-ray diffraction pattern as shown in Figure 1 is outside the scope of the claims.

Regarding the Examiner's assertion that administering a compound to a subject results in the loss of crystalline structure, Applicants note that although crystalline forms of drugs are absorbed into the body through the bloodstream, whereupon they ultimately lose their specific crystalline structure, those skilled in the art recognize that the specific form of a drug may affect its dissolution rate, solubility and bioavailability upon administration to the bloodstream, thereby affecting its therapeutic efficacy. For example, Jain (of record) at p. 316 states that "[t]he polymorphs show different solubilities and rates of solution, hence different absorption (bioavailability) tendencies." Muzaffar (of record) at p. 59 gives specific examples of drugs whose absorption and therapeutic efficacy are dependent upon their solid-state form (*e.g.*, crystalline form I v. crystalline form II v. amorphous; anhydrous v. hydrate v. solvate). As pointed out above, any esomeprazole magnesium trihydrate administered to a subject not having substantially the same X-ray diffraction pattern as shown in Figure 1 is simply outside the scope of the claims.

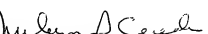
Accordingly, Appellants submit that no case for lack of written description of claims 33 and 34 under § 112, first paragraph, has been made out, and the rejection should not be sustained.

CONCLUSION

Applicants submit that claims 1, 3-9, 11-17, 33 and 34 meet the requirements for patentablility under §§ 102, 103 and 112. Accordingly, reversal of the Examiner's rejections is appropriate and is respectfully solicited.

Respectfully submitted,

Dated: October 3, 2007

BY: 

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CLAIMS APPENDIX

1. A compound which is a crystalline form II of (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium trihydrate, having substantially the same X-ray diffraction pattern as shown in Figure 1.

3. The compound of claim 1, having an X-ray diffraction pattern expressed in terms of 2 theta angles and obtained with a diffractometer equipped with a copper K X-radiation source, wherein said X-ray powder diffraction pattern includes five or more peaks selected from the group consisting of peaks with 2 theta angles of about 4.824, about 5.552, about 7.411, about 8.608, about 12.104, about 14.16, about 18.471, and about 21.089.

4. The compound of claim 1, having an X-ray powder diffraction pattern expressed in terms of 2 theta angles and obtained with a diffractometer equipped with a copper K X-radiation source, wherein said X-ray powder diffraction pattern includes five or more peaks selected from the group consisting of peaks with 2 theta angles of 4.82 ± 0.09, 5.55 ± 0.09, 7.41 ± 0.09, 8.60 ± 09, 12.10 ± 0.09, 14.16 ± 0.09, 18.47 ± 0.09, and 21.08 ± 0.09.

5. The compound of claim 4, wherein the X-ray powder diffraction pattern includes peaks with 2 theta angles of about 4.82, about 5.55, about 7.41, about 8.60, about 12.10, about 14.16, about 18.47, and about 21.09.

6. A composition comprising (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium trihydrate, wherein at least

75% of said (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium is a crystalline form II of (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium trihydrate, having substantially the same X-ray diffraction pattern as shown in Figure 1.

7. The composition of claim 6, wherein at least 90% of said (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium is the crystalline form II of (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium.

8. The composition of claim 7, wherein at least 95% of said (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium is the crystalline form II of (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium.

9. The composition of claim 6, which is substantially free of other forms of (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium.

11. The composition of claim 6, which has a moisture content of from about 2% to about 10% as measured by the Karl Fischer method.

12. The composition of claim 11, which has a moisture content of from about 7% to about 8% as measured by the Karl Fischer method.

13. The composition of claim 6, wherein 20% or less by weight of the solid (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium is in an amorphous form.

14. The composition of claim 13, wherein 10% or less by weight of the solid (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium is in an amorphous form.

15. The composition of claim 14, wherein 5% or less by weight of the solid (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium is in an amorphous form.

16. The composition of claim 15, wherein 1% or less by weight of the solid (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium is in an amorphous form.

17. The composition of claim 16, wherein said solid (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium is substantially free of the amorphous form of (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium.

33. A pharmaceutical composition comprising a crystalline form II of (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium trihydrate, having substantially the same X-ray diffraction pattern as shown in Figure 1, and a pharmaceutically acceptable carrier.

34. A method for reducing gastric acid secretion in a subject which comprises administering to the subject a solid pharmaceutical composition comprising an amount of a crystalline form II of (S)-5-methoxy-2-[[4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole magnesium trihydrate, having substantially the same X-ray diffraction pattern as shown in Figure 1, effective to reduce gastric acid secretion by said subject.

EVIDENCE APPENDIX

None.

RELATED PROCEEDINGS APPENDIX

None.